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| <b>U. S. PATENT AND TRADEMARK OFFICE</b><br><b>U.S. DEPARTMENT OF COMMERCE</b><br><br><b>TRANSMITTAL LETTER TO THE UNITED STATES</b><br><b>DESIGNATED/ELECTED OFFICE (DO/EO/US)</b><br><b>CONCERNING A FILING UNDER 35 U.S.C. 371</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                      | <b>ATTORNEY'S DOCKET NUMBER</b><br>T1650P<br><br><b>U.S. APPLICATION NO. (If known, see 37 CFR 1.5)</b><br><div style="font-size: 1.5em; font-weight: bold;">10/581291</div> |
| <b>INTERNATIONAL APPLICATION NO.</b><br>PCT/GB2004/005234                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | <b>INTERNATIONAL FILING DATE</b><br>14 December 2004 | <b>PRIORITY DATE CLAIMED</b><br>18 December 2003                                                                                                                             |
| <b>TITLE OF INVENTION</b><br>TREATMENT FOR ALZHEIMER'S DISEASE AND RELATED CONDITIONS                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                      |                                                                                                                                                                              |
| <b>APPLICANT(S) FOR DO/EO/US</b><br>Jose Luis Castro Pineiro                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                      |                                                                                                                                                                              |
| <p><b>Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:</b></p> <ol style="list-style-type: none"> <li>1. <input checked="" type="checkbox"/> This is a <b>FIRST</b> submission of items concerning a filing under 35 U.S.C. 371.</li> <li>2. <input type="checkbox"/> This is a <b>SECOND</b> or <b>SUBSEQUENT</b> submission of items concerning a filing under 35 U.S.C. 371.</li> <li>3. <input type="checkbox"/> This is an express request to begin national examination procedures [35 U.S.C. 371(f)]. The submission must include items (5), (6), (9) and (21) indicated below.</li> <li>4. <input checked="" type="checkbox"/> The US has been elected (PCT Article 31).</li> <li>5. <input checked="" type="checkbox"/> A copy of the International Application as filed [35 U.S.C. 371(c)(2)]           <ol style="list-style-type: none"> <li>a. <input checked="" type="checkbox"/> is attached hereto (required only if not communicated by the International Bureau).</li> <li>b. <input type="checkbox"/> has been communicated by the International Bureau.</li> <li>c. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US).</li> </ol> </li> <li>6. <input type="checkbox"/> An English language translation of the International Application as filed [35 U.S.C. 371(c)(2)].           <ol style="list-style-type: none"> <li>a. <input type="checkbox"/> is attached hereto</li> <li>b. <input type="checkbox"/> has been previously submitted under 35 U.S.C. 154(d)(4).</li> </ol> </li> <li>7. <input type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 [35 U.S.C. 371(c)(3)].           <ol style="list-style-type: none"> <li>a. <input type="checkbox"/> are attached hereto (required only if not communicated by the International Bureau).</li> <li>b. <input type="checkbox"/> have been communicated by the International Bureau.</li> <li>c. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired.</li> <li>d. <input type="checkbox"/> have not been made and will not be made.</li> </ol> </li> <li>8. <input type="checkbox"/> An English language translation of the amendments to the claims under PCT Article 19 [35 U.S.C. 371(c)(3)].</li> <li>9. <input checked="" type="checkbox"/> An oath or declaration of the inventor(s) [35 U.S.C. 371(c)(4)].</li> <li>10. <input type="checkbox"/> An English language translation of the annexes of the International Preliminary Examination Report under PCT Article 36 [35 U.S.C. 371(c)(5)].</li> </ol> <p><b>Items 11 to 20 below concern other document(s) or information included:</b></p> <ol style="list-style-type: none"> <li>11. <input checked="" type="checkbox"/> An Information Disclosure Statement under 37 CFR 1.97 and 1.98.</li> <li>12. <input type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.</li> <li>13. <input checked="" type="checkbox"/> A preliminary amendment.</li> <li>14. <input type="checkbox"/> An Application Data Sheet under 37 CFR 1.76.</li> <li>15. <input type="checkbox"/> A substitute specification.</li> <li>16. <input type="checkbox"/> A power of attorney and/or change of address letter.</li> <li>17. <input type="checkbox"/> A computer-readable form of the sequence listing in accordance with PCT Rule 13ter, 2 and 37 CFR 1.821 - 1.825.</li> <li>18. <input type="checkbox"/> A second copy of the published International Application under 35 U.S.C. 371(c)(2).</li> <li>19. <input type="checkbox"/> A second copy of the English language translation of the international application under 35 U.S.C. 371(c)(2).</li> <li>20. <input type="checkbox"/> Other items or information:</li> </ol> |                                                      |                                                                                                                                                                              |

**EXPRESS MAIL CERTIFICATE**  
**DATE OF DEPOSIT** June 1, 2006  
**EXPRESS MAIL NO.** EV 660608126 US  
**THESE CERTIFY THAT THIS CORRESPONDENCE IS**  
**BEING DEPOSITED WITH THE UNITED STATES POSTAL**  
**SERVICE AS EXPRESS MAIL "POST OFFICE TO ADDRESSEE"**  
**ON THE ABOVE DATE IN AN ENVELOPE ADDRESSED TO**  
**COMMISSIONER FOR PATENTS, P.O. BOX 1450,**  
**ALEXANDRIA, VIRGINIA 22313-1450**  
**MAILED BY** Harry J. Crowley  
**DATE** 6/1/06

AP20 Rec'd PCT/PTO 01 JUN 2006

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |              |                                                                               |            |                                    |              |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------|-------------------------------------------------------------------------------|------------|------------------------------------|--------------|
| U.S. APPLICATION NO. (If known, see 37 CFR 1.5)<br><b>10/581291</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |              | INTERNATIONAL APPLICATION NO.<br>PCT/GB2004/005234                            |            | ATTORNEY'S DOCKET NUMBER<br>T1650P |              |
| The following fees are submitted:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |              |                                                                               |            | CALCULATIONS                       | PTO USE ONLY |
| 21. <input checked="" type="checkbox"/> Basic national fee.....\$300                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |              |                                                                               |            | \$300.00                           |              |
| 22. <input checked="" type="checkbox"/> Examination fee (37 CFR 1.492(c))<br>If the written opinion prepared by ISA/US or the international preliminary examination report prepared by IPEA/US indicates all claims satisfy provisions of PCT Article 33(1)-(4).....\$0<br>All other situations.....\$200                                                                                                                                                                                                                                                                                                 |              |                                                                               |            | \$200.00                           |              |
| 23. <input checked="" type="checkbox"/> Search fee (37 CFR 1.492(b))<br>If the written opinion of the ISA/US or the international preliminary examination report prepared by IPEA/US indicates all claims satisfy provisions of PCT Article 33(1)-(4).....\$0<br>Search fee [37 CFR 1.445(a)(2)] has been paid on the international application to the USPTO as an International Searching Authority.....\$100<br>International Search Report prepared by an ISA other than the US and provided to the Office or previously communicated to the US by the IB .....\$400<br>All other situations.....\$500 |              |                                                                               |            | \$400.00                           |              |
| TOTAL OF 21, 22 and 23=                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |              |                                                                               |            | \$900.00                           |              |
| <input type="checkbox"/> Additional fee for specification and drawings filed in paper over 100 sheets (excluding sequence listing or computer program listing filed in an electronic medium). The fee is \$250 for each additional 50 sheets of paper or fraction thereof.                                                                                                                                                                                                                                                                                                                                |              |                                                                               |            |                                    |              |
| Total Sheets                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Extra Sheets | Number of each additional 50 or fraction thereof (round up to a whole number) | RATE       |                                    |              |
| 21 - 100 =                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 0 /50        | 0 = 0                                                                         | X \$250.00 | \$0.00                             |              |
| Surcharge of \$130.00 for furnishing the oath or declaration later than 30 months from the earliest claimed priority date [37 CFR 1.492(e)].                                                                                                                                                                                                                                                                                                                                                                                                                                                              |              |                                                                               |            |                                    |              |
| CLAIMS                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | NUMBER FILED | NUMBER EXTRA                                                                  | RATE       |                                    |              |
| Total Claims                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 8 - 20 =     | 0                                                                             | X \$50.00  | \$0.00                             |              |
| Independent Claims                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 2 - 3 =      | 0                                                                             | X \$200.00 | \$0.00                             |              |
| MULTIPLE DEPENDENT CLAIM(S) (if applicable)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |              |                                                                               | + \$360.00 | \$0.00                             |              |
| TOTAL OF ABOVE CALCULATIONS (SUBTOTAL)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |              |                                                                               |            | \$900.00                           |              |
| Processing fee of \$130.00 for furnishing the English translation later than 30 months from the earliest claimed priority date (37 CFR 1.492(f)).                                                                                                                                                                                                                                                                                                                                                                                                                                                         |              |                                                                               |            | +                                  |              |
| TOTAL NATIONAL FEE                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |              |                                                                               |            | =                                  | \$900.00     |
| Fee for recording the enclosed assignment [37 CFR 1.21(h)]. The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property.                                                                                                                                                                                                                                                                                                                                                                                                                                   |              |                                                                               |            | +                                  |              |
| TOTAL FEES ENCLOSED                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |              |                                                                               |            | =                                  | \$900.00     |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |              |                                                                               |            | Amount to be refunded:             |              |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |              |                                                                               |            | Amount to be charged:              |              |
| a. <input type="checkbox"/> A check in the amount of \$ _____ to cover the above fees is enclosed.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |              |                                                                               |            |                                    |              |
| b. <input checked="" type="checkbox"/> Please charge my Deposit Account No. <u>13-2755</u> in the amount of <u>\$900.00</u> to cover the above fees.<br>A duplicate copy of this sheet is enclosed.                                                                                                                                                                                                                                                                                                                                                                                                       |              |                                                                               |            |                                    |              |
| c. <input checked="" type="checkbox"/> The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to the Deposit Account No. <u>13-2755</u> . A duplicate copy of this sheet is enclosed.                                                                                                                                                                                                                                                                                                                                                       |              |                                                                               |            |                                    |              |
| NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive [37 CFR 1.137(a) or (b)] must be filed and granted to restore the International Application to pending status.                                                                                                                                                                                                                                                                                                                                                                                   |              |                                                                               |            |                                    |              |
| SEND ALL CORRESPONDENCE TO:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |              |                                                                               |            |                                    |              |
| Customer No. 000210                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |              |                                                                               |            |                                    |              |
| MERCK & CO., INC.<br>Patent Department, RY60-30<br>P.O. Box 2000<br>126 East Lincoln Avenue<br>Rahway, New Jersey 07065-0970                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |              |                                                                               |            |                                    |              |
| DATE: <u>June 1, 2006</u>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |              |                                                                               |            |                                    |              |
| PHONE #: <u>(732) 594-3904</u>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |              |                                                                               |            |                                    |              |
| <br>SIGNATURE                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |              |                                                                               |            |                                    |              |
| J. Eric Thies<br>NAME                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |              |                                                                               |            |                                    |              |
| 35,382<br>REGISTRATION NUMBER                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |              |                                                                               |            |                                    |              |